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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,245	06/24/2002	Johan - Valentin Kahl	GRUNP118	9295
49691	7590	09/19/2005	EXAMINER	
IP STRATEGIES			BARTON, JEFFREY THOMAS	
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SUITE I			ART UNIT	PAPER NUMBER
ASHEVILLE, NC 28801			1753	
DATE MAILED: 09/19/2005				

Please find below and/or attached an Office communication concerning this application or proceeding.

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<b>Office Action Summary</b>	Application No.	Applicant(s)	
	10/049,245	KAHL ET AL.	
	Examiner Jeffrey T. Barton	Art Unit 1753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 30 June 2005.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 47-84 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) 47-66 is/are allowed.
- 6) Claim(s) 67-84 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) All    b) Some \* c) None of:
    1. Certified copies of the priority documents have been received.
    2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
	6) <input type="checkbox"/> Other: _____

## DETAILED ACTION

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 30 June 2005 has been entered.

### ***Response to Amendment***

2. The amendment filed on 30 June 2005 does not place the application in condition for allowance.

### ***Status of Rejections Pending Since the Office Action of 2 March 2005***

3. All rejections of claims 47-66 are withdrawn due to Applicant's amendment.
4. The rejection of claims 67-70, 72, and 75 under 35 U.S.C. §102(e) as anticipated by Stowell et al is withdrawn due to Applicant's amendment.
5. The rejection of claims 67, 69, 70, 72, 73, and 75 under 35 U.S.C. §102(b) as anticipated by Peterson is withdrawn due to Applicant's amendment.
6. All other prior rejections are maintained.

***Claim Rejections - 35 USC § 112***

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 82-84 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is no disclosure in the specification regarding "non-specifically binding" the particles to be analyzed, as required in these claims.

***Claim Rejections - 35 USC § 103***

9. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

10. Claims 67, 69-72, 75-78, 80, and 81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Groves et al in view of Goodrich, Jr. et al.

Regarding claims 67, 69-72, and 75, Groves et al disclose a microchannel electrophoresis chamber (Figure 2 and caption; the thickness of the membrane/fluid layer is disclosed as 10-50 micrometers; since the volume defined between the two coverslips has at least one micrometer-scale dimension, it reads on a "microchannel",

broadly defined) comprising a channel having a bottom surface including a substrate-supporting membrane (Pages 2717-2718 - Supported bilayers section, also Figure 2 and caption)

Regarding claim 76, Groves et al disclose the microchannel chamber being connected to an electrode assembly. (Figure 2)

Regarding claim 77, this channel is 10 mm wide.

Regarding claim 78, the channel depth is disclosed as 10-50 microns. (Figure 2 caption)

Regarding claims 80 and 81, the electrodes pictured in Figure 2a are on the longitudinal ends of the channel, and extend longitudinally in the direction of the channel from either end.

Groves et al do not explicitly disclose drying the membrane.

Goodrich et al disclose a method of freeze-drying such lipid membranes for storage and later use. (Column 4, lines 46-61)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the devices of Groves et al by freeze-drying the membrane sandwiches for later use, as taught by Goodrich et al, because it would allow a researcher to choose when to use a membrane, as opposed to needing to prepare a freshly prepared membrane for each experiment, and Goodrich et al teach the usefulness of the method in storing synthetic phospholipid membranes. (Column 4, lines 46-55)

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11. Claims 67, 69, 70, and 72-80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boxer et al in view of Goodrich, Jr. et al.

Regarding claims 67, 69, 70, 72, and 75, Boxer et al disclose lipid bilayer membranes comprising proteins that are supported on glass coverslips (Column 7, lines 20-40), with barriers (28) that divide the membrane and can extend above the substrate to a height of several micrometers. (Column 5, lines 59-64) The areas between these barriers can thus be called "microchannels", given this microscale dimension.

Regarding claims 73 and 74, Boxer et al disclose the support comprising PMMA. (Column 10, lines 4-11)

Regarding claim 76, Boxer et al disclose the microchannel chamber being connected to an electrode assembly. (e.g. Figure 5)

Regarding claim 77, the supports (and therefore channels) are disclosed as having dimensions as low as 5 mm per side. (Column 5, lines 41-43)

Regarding claim 78, the disclosed bilayer and aqueous film thickness would result in a channel of this depth. (Column 5, lines 50-64)

Regarding claim 79, Boxer et al disclose two-dimensional arrays of membrane sections, which could be called channels. (e.g. Figure 2, Column 8, lines 43-52)

Regarding claim 80, the electrodes pictured in Figure 5 are on the longitudinal ends of the channel.

Boxer et al do not explicitly disclose drying the membrane.

Goodrich et al disclose a method of freeze-drying such lipid membranes for storage and later use. (Column 4, lines 46-61)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the devices of Boxer et al by freeze-drying the membranes for later use, as taught by Goodrich et al, because it would allow a researcher to choose when to use a membrane, as opposed to needing to prepare a freshly prepared membrane for each experiment, and Goodrich et al teach the usefulness of the method in storing synthetic phospholipid membranes. (Column 4, lines 46-55)

12. Claims 67, 69-72, 75-78, 80, and 81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Groves et al in view of Hianik et al.

The disclosure of Groves et al is as described above in paragraph 10.

Groves et al do not explicitly disclose drying the membrane.

Hianik et al disclose preservation and storage of a dried substrate-supported lipid bilayer membrane, with recovery of membrane parameters upon rehydration. (Abstract; Results and discussion)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the devices of Groves et al by dehydrating the membrane sandwiches for later use, as taught by Hianik et al, because it would allow a researcher to choose when to use a membrane, as opposed to needing to prepare a freshly prepared membrane for each experiment. The convenience of this would have been obvious and highly desirable to a skilled artisan, and is described by Hianik et al in the first paragraph of their Introduction.

13. Claims 67, 69, 70, and 72-80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boxer et al in view of Hianik et al.

The disclosure of Boxer et al is as described above in paragraph 11.

Boxer et al do not explicitly disclose drying the membrane.

Hianik et al disclose preservation and storage of a dried substrate-supported lipid bilayer membrane, with recovery of membrane parameters upon rehydration. (Abstract; Results and discussion)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the devices of Boxer et al by dehydrating the membranes for later use, as taught by Hianik et al, because it would allow a researcher to choose when to use a membrane, as opposed to needing to prepare a freshly prepared membrane for each experiment. The convenience of this would have been obvious and highly desirable to a skilled artisan, and is described by Hianik et al in the first paragraph of their Introduction.

14. Claim 68 is rejected under 35 U.S.C. 103(a) as being unpatentable over Groves et al and Goodrich, Jr. et al as applied to claim 67 above, and further in view of Bailey et al.

Groves et al and Goodrich et al disclose a combination as described above in addressing claim 67.

Neither Groves et al nor Goodrich et al explicitly disclose a membrane comprising cationic lipids.

Bailey et al disclose preparation of liposomes comprising bilayers including cationic lipids. (Abstract)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combination of Boxer et al and Goodrich et al by using bilayers comprising cationic lipids, as taught by Bailey et al, because Bailey et al teach their ability to form bilayers and the function of the cationic lipid in promoting liposome fusion.

15. Claim 68 is rejected under 35 U.S.C. 103(a) as being unpatentable over Boxer et al and Goodrich, Jr. et al as applied to claim 67 above, and further in view of Bailey et al.

The reasoning for this rejection parallels that given above in paragraph 14.

16. Claim 68 is rejected under 35 U.S.C. 103(a) as being unpatentable over Groves et al and Hianik et al as applied to claim 67 above, and further in view of Bailey et al.

The reasoning for this rejection parallels that given above in paragraph 14.

17. Claim 68 is rejected under 35 U.S.C. 103(a) as being unpatentable over Boxer et al and Hianik et al as applied to claim 67 above, and further in view of Bailey et al.

The reasoning for this rejection parallels that given above in paragraph 14.

***Allowable Subject Matter***

18. Claims 47-66 are allowed.
19. The following is an examiner's statement of reasons for allowance:

The reason for indicating these claims as allowable is the inclusion of the limitation in lines 12-14 of the claim that the substrate "has a structured membrane-compatible surface that provides a force acting on the moving particles that depends on the length of the particles." Boxer et al disclose using a particle size-dependent force provided by obstacles (Embodiment of Figure 5), but the obstacles are formed from a material that is not membrane-compatible, as breaks in the membrane are produced by its presence. (see Figure 1) In contrast, the instant claims require that the structured membrane-compatible surface itself provide the force on the particles. Groves et al use obstacles formed by scratching the coverslip to guide the migration of particles on a supported membrane (e.g. Figure 4), but these would also appear to break the membrane, and Groves et al do not disclose or suggest that the confining force would depend on particle length. No suggestion or motivation was found in the prior art to modify these methods, and it is not clear that such modification would be possible.

The above limitation is optional in claim 47 (See lines 7-16), but no prior art was found that anticipated or rendered obvious the other electrophoresis option (Lines 8-10) of modifying the strength or direction of the electric field during separation of the particles on the membrane.

Therefore, the claims are considered to patentably distinguish over the prior art.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

***Response to Arguments***

20. Applicant's arguments filed 30 June 2005 concerning the rejection of claims 67-81 have been fully considered but they are not persuasive.

Applicant considers the combination of art used in rejecting these claims to have been "unmotivated and possibly unworkable." (Page 26, 1<sup>st</sup> paragraph) No convincing arguments to this effect have been presented by Applicant. Applicant specifically asserts that the application of the teachings of Goodrich to those of either Groves et al or Boxer et al would be problematic, since the additives used by Goodrich might interfere with electrophoresis, and points out that no motivation for combination is present in the cited references.

Goodrich teaches freeze-drying of lipid membranes for later use, using a cryoprotectant medium comprising polysaccharides. (see Claims) Applicant claims that this additive would modify the results of electrophoresis (Paragraph bridging Pages 20 and 21), but it is not clear to the Examiner that any significant interference would be expected, such that the addition of polysaccharides would be avoided by a skilled artisan.

Applicant also seems to believe that Goodrich is concerned with three-dimensional membrane structures (Paragraph bridging pages 20 and 21), but Goodrich et al specifically discuss the preservation of "synthetic phospholipid membranes or vesicles" (italics added), i.e. two or three-dimensional structures. Indeed, Goodrich et al clearly envision cryoprotection of any lipid membrane material. (Column 4, lines 48-55)

Regarding the question of motivation, the disclosure of Goodrich et al is entirely directed to the preservation of materials with lipid membranes for later use, and specifically preventing damage to the membrane. (e.g. platelet or bone marrow preservation in the Summary section) A skilled artisan would have recognized that such preservation would be equally suited to preservation of supported membranes for later use. The motivation for this combination is not explicitly recited in the references, but lies within the knowledge of a skilled artisan, who would have desired the convenience of having a dried, pre-formed membrane instead of having to individually prepare each membrane prior to use.

### ***Conclusion***

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Jeffrey Barton, whose telephone number is (571) 272-1307. The examiner can normally be reached Monday-Friday from 8:30 am – 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen, can be reached at (571) 272-1342. The fax number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

JTB  
13 September 2005

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